

**P-164/D****P-166****DOES ENVIRONMENTAL PERCHLORATE EXPOSURE ALTER HUMAN THYROID FUNCTION? DETERMINATION OF THE DOSE-RESPONSE FOR INHIBITION OF RADIOIODINE UPTAKE**

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The perchlorate ion ( $\text{ClO}_4^-$ ) is a potent inhibitor of the sodium-iodide symporter. Over the past half-century,  $\text{ClO}_4^-$  at doses of 0.2 to 2 g/day has been utilized in the diagnosis and treatment of thyroid disease.  $\text{ClO}_4^-$  occurs in natural fertilizers and is manufactured for use as a propellant in rocket fuel. Recent improvement in analytical methods has led to widespread detection of  $\text{ClO}_4^-$  in drinking water, with most values  $<20 \mu\text{g/L}$  and almost all values  $<100 \mu\text{g/L}$ , yielding daily doses  $<0.6$  and  $<3 \mu\text{g/kg}$ , respectively. As part of an effort to estimate the risk of thyroid hypofunction from environmental  $\text{ClO}_4^-$  exposure, we gave  $\text{ClO}_4^-$  at one of 3 doses to 24 euthyroid volunteers (4M and 4F per dose; 18-57 yr-old) for 14 days.  $\text{ClO}_4^-$  was dissolved in drinking water to yield a daily dose of 0.02, 0.1, or 0.5 mg/kg (approx. 1.4, 7, or 35 mg assuming 70 kg body wt.) in 400 ml; subjects drank 100 ml at 4 set times throughout each day. Measurement of 8- and 24-hr  $^{123}\text{I}$  thyroid uptakes was performed prior to  $\text{ClO}_4^-$  exposure (baseline), on exposure days 2 and 14, and on post-exposure day 15. Expressed as a percentage of baseline, mean ( $\pm$  SE) 24-hr uptakes in the 0.02, 0.1, and 0.5 mg/kg dose groups were 83 (5.6), 59 (3.5), 31 (2.6) on exposure day 2; 85 (4.5), 57 (4.7), 34 (4.5) on exposure day 14; and 111 (5.1), 96 (12), 108 (12) on post-exposure day 15. A linear log-dose relationship was observed. The 8-hr and 24-hr regression slopes were statistically indistinguishable. There was no M/F difference. Applied to exposure day 14, the 3-dose regression model predicts a no-effect dose (highest non-inhibitory dose) of  $7 \mu\text{g/kg}$  (approx. 0.5 mg) per day. In 4 volunteers subsequently tested at this dose there was no inhibition of uptake, as predicted. The  $\text{ED}_{50}$  (50% effective dose) and maximum effective dose (lowest dose required to suppress uptake completely) are predicted by the 3-dose regression model to be 0.17 and 4.3 mg/kg (approx. 12 and 300 mg) per day, respectively. We are in the process of analyzing data on serum TT4, FT4, TT3, and TSH. Conclusions: We estimate that the no-effect dose of 0.5 mg/day would be consumed in drinking water containing  $\text{ClO}_4^-$  at  $250 \mu\text{g/L}$ . Therefore, water supplies containing less than this should not affect human thyroid function.

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